REMARKS

Interview Summary

As an initial matter, Applicants thank Examiner Schafer for the productive telephonic interview conducted on February 17, 2011. During that interview, the Examiner indicated that the rejection under 35 U.S.C. § 112, second paragraph, would be withdrawn. Regarding the rejection under 35 U.S.C. § 103(a), the Examiner indicated that a declaration showing unexpected results of the claimed invention would be helpful in overcoming the rejection for obviousness. Applicants submit herewith such a declaration as requested by the Examiner.

Office Action Summary

Claims 1-4, 7-10, 12-17, 29-37, 40-44, and 62-68 are pending in the application. Based on the advisory action and the above-described interview, the sole outstanding issues are the rejection of claims 1-4, 7-10, 12-17, and 62-68 under 35 U.S.C. § 103(a) for obviousness.

Rejections under 35 U.S.C. § 103(a)

Claims 1, 16, and 17 were rejected under 35 U.S.C. § 103(a) for obviousness over Clerico et al., J. Endoc. Invest. 21:170-179, 1998, in view of Clerico et al., Clin. Chemistry 46:1529-1534, 2000. Claims 2-4, 7-15, 46, 47, 59, and 60 were rejected for obviousness over Clerico (1998), in view of Clerico (2000), and further in view of Buechler et al., U.S. Patent No. 7,341,838.

Applicants maintain the position that the Office has failed to make a *prima facie* case of obviousness and hereby incorporate by reference arguments against obviousness made in the Reply to Final Office action filed September 7, 2010. Furthermore, Applicants, at the invitation of the Office, submit herewith evidence that the determination of activation of ANP and BNP without measuring the individual levels of proANP and proBNP results in an unexpectedly superior clinical method. These data, provided by Professor Vuolteenaho and Professor Ruskoaho in the accompanying declaration, are objective evidence of non-obviousness.

As stated by Professors Vuolteenaho and Ruskoaho, the present invention includes detection of:

> activation or inactivation of the ANP and BNP hormonal systems by assaying for both proANP- and proBNP- derived peptides in the same sample, at the same time, in a single reading, in a single assay. Practical tests of our present invention showed that it does not simply replicate the function of two separate assays...The method produces a single result, does not require sophisticated data extraction, and is simpler to perform than prior art methods. Small increases of only NT-proBNP are masked by the high basal levels of NT-proANP, thus decreasing the risk of false positive results. On the other hand, even small increases of both NT-proANP and NT-proBNP can be detected with high sensitivity, thus decreasing the risk of false negative results." (Declaration at paragraph 6).

According to the declaration, "[t]his is illustrated by a practical example in Figure 4/5 of the present application, in which clinical samples of 500 patients with heart failure were measured. Unexpectedly the NT-proXNP value (Figure 4/5, bar on the right) provides a clearly better separation between the different New York Heart Association (NYHA) classes, and thus has more clinical power, as compared to NT-proANP alone (bar on the left), NT-proBNP alone (bar in the middle), or their arithmetic sum, measured from the same samples" (Id. at paragraph 7). Professors Vuolteenaho and Ruskoaho conclude that "[t]hese results are not self-evident and could not have been predicted with prior knowledge without devising the novel method and testing it with actual clinical samples" (Id.). These data showing unexpected results are compelling evidence of the non-obviousness of the claimed invention. In view of this evidence, the rejections for obviousness should be withdrawn.

CONCLUSION

Applicants submit that the claims are in condition for allowance, and such action is respectfully requested. If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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